CLAIMS

1. A method for diagnosing susceptibility to normal pregnancy, pre-eclampsia and/or eclampsia and/or intrauterine growth retardation and/or susceptibility to miscarriage and/or miscarriage-related infertility comprising the steps of:

a) obtaining a fluid and/or tissue sample from a female and/or male and/or foetus; and either

b) determining the sequence of all or part of the HLA-G nucleic acid, and/or HLA-G linked nucleic acid; or

c) detecting variant forms of all or part of the HLA-G protein, and/or proteins encoded by HLA-G linked genes or:

d) measuring the functional activity of all or part of the HLA-G encoding protein and/or proteins encoded by HLA-G linked genes or:

e) measuring the size and /or level of all or part of HLA-G mRNA or mRNA transcribed from HLA-G linked genes or:

f) measuring the size and /or level of all or part of HLA-G protein and/or protein encoded by HLA-G linked genes or:

g) quantifying cells or molecules whose concentration changes as a result of HLA-G action; and

h) comparing any of the parameters b) to g) with those of a female and/or male and/or foetus of a normal pregnancy and/or a pregnancy with pre-eclampsia and/or eclampsia and/or intrauterine growth retardation and/or susceptibility to miscarriage and/or miscarriage-related fertility outcome.

2. A method as claimed in claim 1 wherein the HLA-G nucleic acid is analysed for the presence of the C and/or T allele of codon 93 in exon 3 and/or the insertion and/or deletion allele of exon 8.

3. A method as claimed in claim 1 wherein the effect of one or more of the HLA-G sequence variants on the functional activity of HLA-G and / or on the size and /or level of all or part of HLA-G mRNA and/or its encoded polypeptide is measured.

4. A method as claimed in claim 1 or 2 wherein all or part of any HLA-G sequence and/or HLA-G linked sequences is amplified, preferably by a method or combination of methods selected from the polymerase chain reaction, nucleic acid sequence based amplification, self sustained sequence replication, transcription-mediated amplification, strand displacement amplification, and the ligase chain reaction.

5. A method as claimed in claim 1-4 wherein comparing of one or more variants identified is performed by association and/or linkage analysis and/or transmission analysis.

6. A method as claimed in any preceding claim wherein all or part of the HLA-G sequence is cloned into a vector.

7. A method as claimed in any preceding claim wherein all or part of the nucleic acid sequence is identified by a method or combination of methods selected from DNA sequencing, glycosylase mediated polymorphism detection, restriction fragment length polymorphism analysis, enzymatic or chemical cleavage analysis, hybridisation to DNA and /or RNA probes and /or DNA probe arrays and/or allele specific DNA and /or RNA probes, allele specific amplification analysis, electrophoretic mobility analysis and 5' nuclease assay analysis.

8. A method as claimed in any preceding claim wherein all or part of HLA-G and /or all or part of one or more variants thereof is expressed as a polypeptide *in vitro* and/or in a prokaryotic and / or eukaryotic cell.

9. A method as claimed in claim 1 wherein the cells of step (g) are blood mononuclear cells and / or T cell and /or natural killer cell subsets thereof and/or HLA-G expressing cells.

10. A method as claimed in any preceding claim wherein the activity of HLA-G and/or any combination of variants thereof and/or blood mononuclear cells and /or a subset of such cells, selected from T cells and/or natural killer cells, is measured by one or more of the following procedures:

(a) measuring the interaction of HLA-G and /or variants thereof with blood mononuclear cells and/or subsets thereof by assessing one or more of the following with respect to HLA-G expressing cells and /or blood mononuclear cells; cell proliferation, transformation, cytotoxic response, surface marker expression, cytokine production, conjugate formation and target specificity,

(b) measuring the size and / or level of all or part of HLA-G mRNA and/or its encoded polypeptide,

(c) measuring the peptide binding capability of all or part of HLA-G and /or variants thereof,

(d) measuring the binding capability of all or part of the HLA-G and /or variants thereof to a HLA-G receptor,

(e) measuring one or more molecules whose level is altered as a result of the interaction of the HLA-G and /or variants thereof and /or cells expressing HLA-G with blood mononuclear cells,

(f) measuring the expression levels of one or more genes and/or proteins in the HLA-G expressing cells.

11. A method as claimed in any preceding claim wherein blood mononuclear cells and/or subsets thereof and/or HLA-G and/or HLA-G linked variants thereof and/or cells expressing all or part of the variants fully and/or partially matching a female and/or male and/or foetus are selected from a test panel.

12. A method as claimed in any preceding claim wherein the HLA-G is partially or fully purified from a cell expressing HLA-G.

13. A method as claimed in any preceding claim wherein the HLA-G is detected by immunoassay using one or more antibodies specific for HLA-G and/or variants thereof.

14. A method as claimed in any preceding claim wherein all or part of the HLA-A, HLA-B, HLA-C, HLA-E, HLA-F and HLA-H genes are analysed in the female and/or male and/or foetus.

15. A method as claimed in claim 1 wherein the molecules of step (g) are selected from IL-1 beta, IL-2, IL-3, IL-4, IL-6, IL-10 and tumour necrosis factor-alpha, or trophoblast specific markers selected from cytokeratins, pregnancy specific glycoprotein 1, human chorionic gonadotrophin and human placental lactogen.

16. A method for screening for agents which can potentially be used as diagnostic indicators and/or drug targets for pre-eclampsia, miscarriage, miscarriage-related infertility and intrauterine growth retardation by:

a) measuring the expression level of one or more genes and/or proteins in HLA-G expressing cells and/or blood mononuclear cells and/or T cell and/or natural killer cells subsets thereof following interaction with HLA-G and/or HLA-G expressing cells;

b) comparing the expression level identified in step a) with the expression level in HLA-G expressing cells and/or the blood mononuclear cells and/or T cell and/or natural killer cell subsets thereof following interaction with HLA-G and/or HLA-G expressing cells in normal pregnancy and/or pre-eclampsia pregnancy and/or intrauterine growth retardation pregnancy and/or miscarriage pregnancy and/or miscarriage-related infertility.

17. A method as claimed in claim 10 or 16 wherein gene expression and/or protein expression is measured by any one or combination of methods selected from hybridisation between cDNA and/or RNA from the cells and DNA probes and/or RNA probes and/or nucleic acid probe arrays, quantitative amplification methods, reverse transcriptase - polymerase chain reaction (RT-PCR), 5' nuclease assay, ribonuclease protection assay and S1 nuclease assay, one dimensional and/or two dimensional gel electrophoresis and staining of proteins, detection of one or more proteins using, enzyme linked immunosorbent assays (ELISA), radioimmunoassays (RIA), protein truncation test (PTT), immunoradiometric assays (IRMA) and immunoenzymatic assays (IEMA), sandwich assays and Western blotting using monoclonal and/or polyclonal antibodies.

18. A pharmaceutical composition comprising a pharmaceutically effective amount of HLA-G and/or cells expressing HLA-G and/or one or more peptides which binds to HLA-G, blood mononuclear cells from a donor and/or test panel known to interact with HLA-G variants, cytokines and any combination thereof including IL-1 beta, IL-2, IL-3, IL-4, IL-6, IL-10 and tumour necrosis factor-alpha and/or